March 4, 2005

Janet M. Mostowy, Ph.D.
Vice President
Product Safety & Regulatory Affairs
Bayer CropScience LP
100 Bayer Road, Building #5
Pittsburgh, PA 15205-9741

Dear Dr. Mostowy:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone posted on the ChemRTK HPV Challenge Program Web site on February 25, 2004. I commend Bayer CropScience LP for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Bayer CropScience advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
1-(4-Chlorophenyl)-4,4-dimethyl-3-pentanone

Summary of EPA Comments

The sponsor, Bayer CropScience LP, submitted a test plan and robust summaries to EPA for 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone (CAS No. 66346-01-8) dated December 29, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on February 25, 2004.

EPA has reviewed this submission and reached the following conclusions:

1. Physicochemical Properties. The melting point, vapor pressure, partition coefficient, and water solubility data are adequate for the purposes of the HPV Challenge Program. The submitter needs to check the accuracy of the boiling point value.

2. Environmental Fate. Data are adequate for the purposes of the HPV Challenge Program.

3. Health Effects. The acute toxicity data are adequate, but the submitter needs to address deficiencies in the robust summaries. The submitter's proposal for reduced health testing based on a closed-system intermediate (CSI) claim was not adequately supported. Thus, there are data gaps for repeated-dose, genetic (chromosome aberrations), and reproductive/developmental toxicity.

4. Ecological Effects. The acute fish and invertebrate toxicity data are adequate for the purposes of the HPV Challenge Program. The algal toxicity data are inadequate. EPA recommends that the submitter provide measured data on an analog or conduct testing on the sponsored chemical.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone Challenge Submission

General

The submitter included a separate, confidential business information (CBI) claim that the sponsored chemical was a closed-system intermediate. EPA reviewed this information and determined that the claim was not supported.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The melting point, vapor pressure, partition coefficient, and water solubility data are adequate for the purposes of the HPV Challenge Program.

Boiling Point. The submitter provided a boiling point value of 178 °C at 0.046 hPa (0.0345 mm Hg). EPA used this value to estimate (via the NOMO5 program) a boiling point of 460 °C at 760 mm Hg. EPA considers this value to be too high. From the submitter's vapor pressure data at various temperatures, however, EPA calculated boiling point values of 303.9 °C, 299.4 °C, and 298.7 °C at 760 mm Hg, values that seem more reasonable. The submitter needs to check the accuracy of its submitted value and provide one at 760 mm Hg.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Available data for these endpoints are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The acute toxicity data are adequate. Data are inadequate for repeated-dose toxicity, reproductive/ developmental toxicity, gene mutations, and chromosomal aberrations. EPA agrees with the submitter that testing is needed for chromosomal aberrations and developmental toxicity. EPA has determined that the submitter's Closed System Intermediate claim (submitted as CBI; analysis not shown here) was not adequately supported (the submitter needs to consult the Guidance for Testing Closed System Intermediates at http://www.epa.gov/chemrtk/guidocs.htm). Thus EPA recommends that the submitter conduct testing according to OECD TG 422 to address the repeated-dose and reproductive/developmental toxicity endpoints.

Genetic Toxicity – Gene Mutations. The summary for a negative reverse mutation assay in *Salmonella typhimurium* is inadequate. The estimated Henry's Law constant of 1.51×10^{-2} atm-m^3/mole (EPIWIN) suggests the potential for volatilization from the test vessels. The submitter did not state whether the study was conducted in a closed system with analytical monitoring of exposure concentrations. If the test was not conducted under these conditions, the submitter needs to provide other gene mutation data or conduct a new test.

Genetic Toxicity – Chromosomal Aberrations. If the chemical is to be tested *in vitro*, the submitter needs to use a closed system with no head space and analytically monitor the chemical concentrations.

Ecotoxicity (fish, invertebrates, and algae)

Fish, Invertebrates. The acute fish and aquatic invertebrate data are adequate.

Algae. Only ECOSAR data were provided. The sponsor needs to provide existing measured data on an analog or test the sponsored substance according to OECD TG 201.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The submitter needs to report whether or not body weight determinations were made and to tabulate toxicity signs by dose level and sex.

Genetic Toxicity – Gene Mutations. The submitter needs to indicate the number of replicates per concentration, criteria for a positive response (i.e., define 'biologically relevant increase'), statistical method used, whether or not cytotoxicity was observed in the repeat study, concentrations tested in the repeat study (instead of a range), and the mean number of revertant colonies per plate for treated and control cultures.

Ecological Effects

Fish and Invertebrates. The submitter needs to identify the method used to measure the chemical in the fish and daphnia assays.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.